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VALECNE ISOMERIZATION OF DIHYDROPYRIDINES

Elliot N. Marvell

Oregon State University
Corvallis, Oregon

August 1967

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Terminal Progress Report

for

Valence Isomerization of Dihydropyridines

PHS 5R01 AM 07771

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Summary

An investigation of the mechanism of the formation of phenylpyridinium ion from König's salt has been carried out. The rate of ring closure in methanol solution was increased by added base. An increase of base concentration increased the rate only up to the point at which the base concentration was equivalent to the salt concentration. The effect was independent of the nature of the base. A mechanism was postulated involving a rate determining valence isomerization of the free base derived from König's salt to a dihydropyridine.

Similar results were shown to pertain with substituted König's salts. Rates were measured for methyl, methoxyl, chloride and fluorine containing salts. As a part of the mechanism a folding and unfolding process for the triene chain of the salt was proposed. This necessarily involves the salt itself rather than the free base derived from it. An investigation of the behavior of the free base in aprotic solvents has been started, but the reactions which take place under these conditions have not been completely identified.

Introduction

The original grant request was in two parts, one involving a synthesis whose key feature was a valence isomerization, a second devoted to the study of the mechanism of the ring opening and ring closure reactions of pyridinium ions. Only the second part was funded. During the first year, Sept. 1, 1963 - Aug. 31, 1964, no predoctoral student was available to work on this project. Thus an extension of time for one year without additional

funds was authorized. The work which is described in this report was done during the period Jan. 1, 1965 - Aug. 31, 1967.

Personnel

During the year September 1, 1963 to August 31, 1964, no predoctoral student was available to work on this grant. The same problem was experienced in September, 1964. Therefore Dr. Gerald Caple was employed full time on this grant from January 1, 1965 to August 31, 1965. He was employed as a postdoctoral research associate during that time. Dr. Caple was born April 3, 1935, in International Falls, Minn. He did his undergraduate studies at St. Olaf College, Northfield, Minn. receiving an A.B. degree in June, 1957. He took his Ph.D. degree in chemistry from Florida State University in June, 1963. His thesis work on Migratory Aptitudes of Unsaturated Groups was under the direction of Prof. Werner Herz. The work was published in J. Org. Chem., 29, 1691 (1964). From September 1, 1964 to December 31, 1965 he was employed as a postdoctoral research associate with Dr. Marvell at Oregon State University. During that time he worked on the valence isomerization of trienes with support from the National Science Foundation. Portions of this work have been published in Tetrahedron Letters 385 (1965) and J. Am. Chem. Soc., 88, 619 (1966).

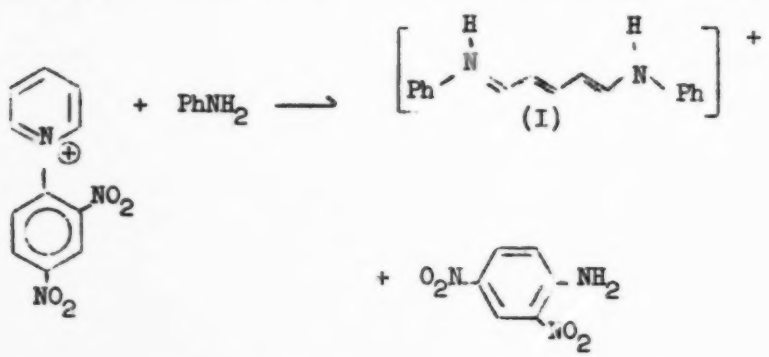
Since September 1, 1965, Mr. Iraj Shahidi has been supported on this grant as a predoctoral research assistant. Mr. Shahidi was born in Tabriz, Iran on May 24, 1941. He did his undergraduate work at UCLA and received is B.S. degree in June, 1965.

Research Accomplishments

The research work on mechanisms of ring opening and ring closure reactions of pyridinium ions has been mainly concentrated on a detailed study of the mechanism of the formation of phenylpyridinium ion from König's salt. A second, though shorter, period of time was devoted to a study of the influence of substituents on this ring closure process. Work was started on two further points related to this, the reactions of the base form of König's salt in aprotic media and ring closure reactions of some unsymmetrical salts.

A. Mechanism of the Ring Closure of König's Salt.

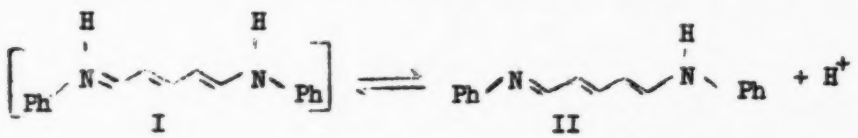
Early in this century Zincke[1] discovered that 2,4-dinitrophenylpyridinium chloride will react with aniline to give a beautifully crystalline deep red salt. He presented evidence to support his assignment of structure I to this salt. Zincke[2] went on to study some of the chemistry of this and related salts. Oddly enough however König[3] found at nearly the



same time that the same salts could be prepared more conveniently by treating pyridine with cyanogen bromide followed by reaction of the initial product with various amines. Thus the salts came to be called after König rather than Zincke. Zincke[1] also called attention to the formation of

phenylpyridinium ion from I when it was heated further with hydrochloric acid or excess aniline. Though many cyanine dyes derived from hydrolysis products of I have been prepared[4] no studies of the mechanisms of the ring-opening or ring-closure processes had been published when we initiated this work.

We chose initially to investigate the ring opening reaction in which 2,4-dinitrophenylpyridinium ion reacts with aniline to give I. In order to study the kinetics it was necessary to provide a homogeneous reaction medium, and methanol was adopted as solvent. A simple mode of analysis for the product appeared to be via ultraviolet spectral methods since I is deeply colored whereas the reactants are only slightly colored at best. The ultraviolet spectrum of I was surprising in that two maxima appear, λ_{max} 405, 485. The relative intensities of the two maxima are concentration dependent, the 405 peak increasing in intensity as the 485 decreases when the solution is made more dilute. This suggested that we might be



observing an equilibrium in which one substance gave rise to two new compounds. One quite reasonable expectation was that the salt I was acting as an acid and was dissociating into the free base II and a hydrogen ion. The 485 peak could be assigned to the acidic salt form and the 405 maximum to the free base. This hypothesis was verified quite simply since addition of excess anilinium ion as an acid removed the 405 peak, while addition of excess triethylamine converted all I to the free base which gave only a single band at 405 mμ.

The intensity of the 405 mμ band is 75,000 and of the 485 mμ band is 105,000. These allow one to measure the dissociation equilibrium constant for $I \rightleftarrows II + H^+$ in methanol. A value of $K = 8.5 \times 10^{-8}$ moles/l. is found. In consideration of the expected rather large loss of delocalization energy in going from I to II, I seems surprisingly acidic. However all of the subsequent experimental results are in keeping with this result.

Our early attempts to study the kinetics of the reaction of 2,4-dinitrophenylpyridinium ion with aniline also led to some unexpected results. In view of the experimental observations reported by Zincke,[1,2] we had fully expected I to be formed at a far greater rate than it decomposed to form phenylpyridinium ion. However it quickly became evident that in methanol solution I was a semi-stable intermediate which was decomposing to phenylpyridinium ion at a rate comparable with its rate of formation. Under such conditions the kinetics of the entire process would be sufficiently complex to render the unraveling of mechanistic detail rather difficult.

Shortly after our observations on the difficulties of isolating the ring opening process had prompted us to look at the ring closure process first, Oda and Mita[5] published a paper describing the study of the kinetics of the ring opening. According to their findings that reaction shows third order kinetics, first order in dinitrophenylpyridinium ion and second order in aniline. Since the rate of the ring closure step is independent of aniline concentration, the ring opening can be studied when the aniline concentration is maintained at sufficiently high levels.

Under non-homogeneous conditions (where the concentrations are sufficiently high so that I^+Cl^-, precipitates) it is possible to prepare

König's salt in quite pure form. Experiments with gram quantities showed that I reacts in methanol solution to form phenylpyridinium chloride and aniline apparently in quantitative yield. We isolated aniline as the benzanilide derivative in 93% yield and phenylpyridinium chloride in ca. 110% of the theoretical. This latter value is always high, apparently due to the difficulty of removing all the solvent from this salt. At 42.6° a dilute solution of I in methanol decomposes with first order kinetics, $k_1 = 8.94 \times 10^{-6}$ sec.$^{-1}$. The rate was determined via an ampule technique and analysis was made by ultraviolet spectral methods after excess anilinium chloride had been added to convert all II in the solution to I. A discussion of the reasons why this reaction gives first order kinetics under these conditions will be made later.

At this point it appeared desirable to study the influence of added anilinium chloride on the reaction rate. However it seemed advisable to do so in a medium of constant ionic strength. Thus we began to study the influence of added neutral salts. The addition of [M] solutions of such salts as lithium chloride gave rise to a strong autocatalysis as is illustrated by a typical run (figure 1). Such a result can only mean that one of the products of the reaction is catalyzing the reaction in the presence of the added salt when it does not do so in the absence of the salt. One possible explanation is that this is a secondary salt effect,[6] and that the equilibrium below is driven to the right by the added salt. Indeed

$$PhNH_2 + I \rightleftharpoons PhNH_3^+ + II$$

addition of a large excess of aniline in the presence of a neutral salt led to a more rapid reaction and the autocatalysis effect was swamped out.

The above explanation for the autocatalysis requires that a base should function as an effective catalyst for the reaction. As the data in Table 1 (runs 16 and 17) clearly show anilinium ion depresses the rate while methoxide ion functions (runs 4-8) as a catalyst. The influence of added methoxide ion shows, however, a curious feature. The rate of the reaction is increased as the concentration of methoxide is increased (concentration of I held constant) up to a point, and thereafter the rate of the reaction is <u>independent</u> of added methoxide ion. The point at which the leveling off sets in is, as far as we have been able to ascertain, when the base concentration reaches the level of the substrate concentration.

As is evident from runs 9-13 a very similar pattern of behavior exists with respect to triethylamine as base. The data also show that in the presence of excess triethylamine the rate plateau is the same as was attained with methoxide ion. Again runs 14 and 15 show that a similar result can be achieved with tri-n-butylamine. This behavior of the weak bases triethylamine and tri-n-butylamine is not due to their generation of methoxide ion via reaction with the solvent. As Table 2 shows the same concentrations of the three bases produce rate increases of comparable magnitude. Also the lack of autocatalysis by aniline in the absence of neutral salts suggests this catalytic activity must be related to the relative base strengths of II vs. the other added bases. This assumption that the role of added base is merely to convert I to II also explains why the weak bases triethylamine and tri-n-butylamine are not quite as effective as is the strong base methoxide ion in increasing the rate of decomposition of I. (Table 2)

The data at this point clearly indicate that the reactive species is the free base II. If we assume this to be the case in the absence of added

base, it is possible to calculate the rate of the reaction of the base in that solution. The mechanism is

$$I \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} II + H^+ \qquad K_1 = \frac{[II][H^+]}{[I]} = 8.5 \times 10^{-8}$$

$$II \xrightarrow{k_2} \text{Prod.}$$

$$\frac{d[\text{Prod}]}{dt} = \frac{k_2 K_1}{[H^+]} [I]$$

assuming [II] is small $\frac{d[\text{Prod}]}{dt} \simeq -\frac{d[I]}{dt}$

hence $k_{obs} = \frac{k_2 K_1}{[H^+]}$

When $[I]_o = 4.1 \times 10^{-4}$ M $\qquad k_{obs} = 8.9 \times 10^{-6}$ sec.$^{-1}$

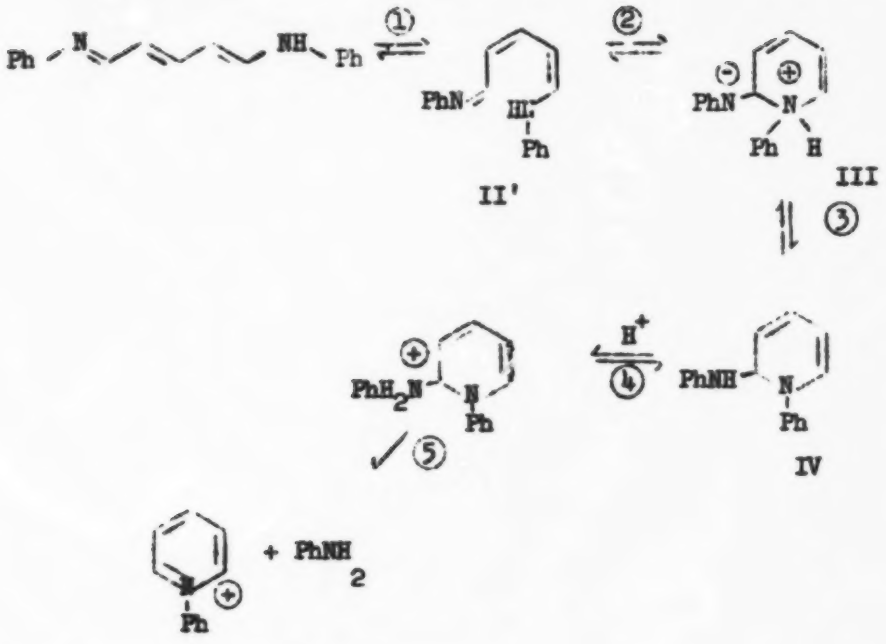
$$k_2 = \frac{k_{obs}[H^+]}{K_1} \qquad [H^+] \simeq 6 \times 10^{-6} \text{ M.}$$

$$k_2 = \frac{(8.9 \times 10^{-6})(6 \times 10^{-6})}{8.5 \times 10^{-8}} = 6.3 \times 10^{-4} \text{ at } 42.6°$$

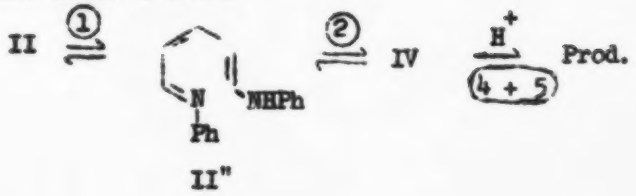
which compares quite favorably with the value of 3.1×10^{-4} at 39.6°. This also makes clear the reasons why approximate first order kinetics are observed in this case. The salt is only 1.5% dissociated initially and at 75% reaction is only 3% dissociated. Thus the fraction of material in the free base form remains virtually constant over the region which was studied kinetically.

At this point only three mechanisms for the conversion of II to phenylpyridinium ion will be considered. These are given below.

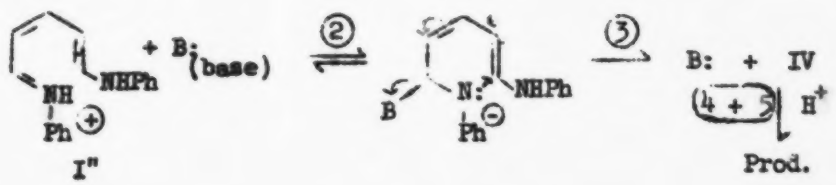
A. Internal nucleophilic addition.



B. Valence isomerization



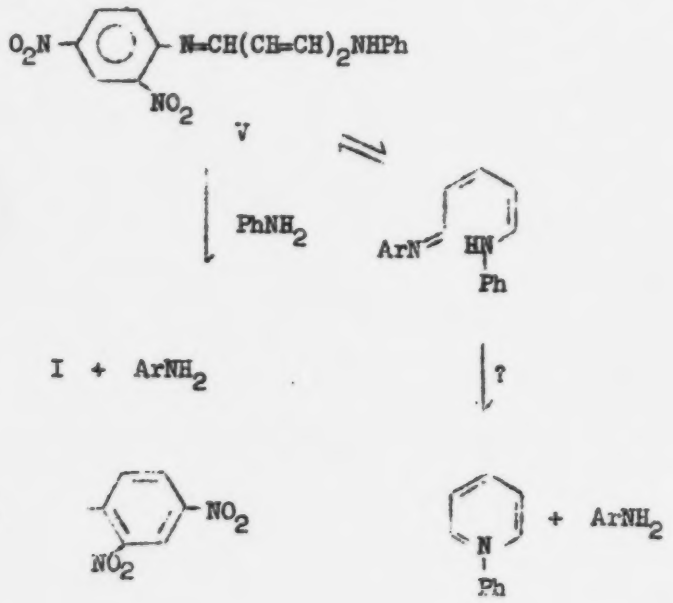
C. Addition-elimination



Of these three it seems easiest to dispose of mechanism C, so it will be considered first. This particular mechanism is an extension of the characteristic addition-elimination sequence for ester or amide hydrolysis.[7]

It can be eliminated here since there seems no simple explanation in terms of this process of the observation that the rate can be independent of the base concentration at high base concentrations. Furthermore, the structure of the base would be expected to cause a large alteration in rate.

It is not so easy to effect a choice between mechanisms A and B. Initially two objections could be raised to process A. It is essentially a process in which a nucleophilic addition to an imino ketone brings about the ring closure. Such reactions generally are acid catalyzed due to the lower susceptibility of the C=N- group to nucleophilic attack.[8] Thus one would suspect that the salt I should be more reactive than the free base II in such a reaction. A second problem concerns the reaction of the probable intermediate V in the ring opening reaction.



Since we were not able to isolate this intermediate despite efforts to do so, it must react rapidly with aniline to form I. However, even in reduced concentrations of aniline (dilute solution) no phenylpyridinium ion appears

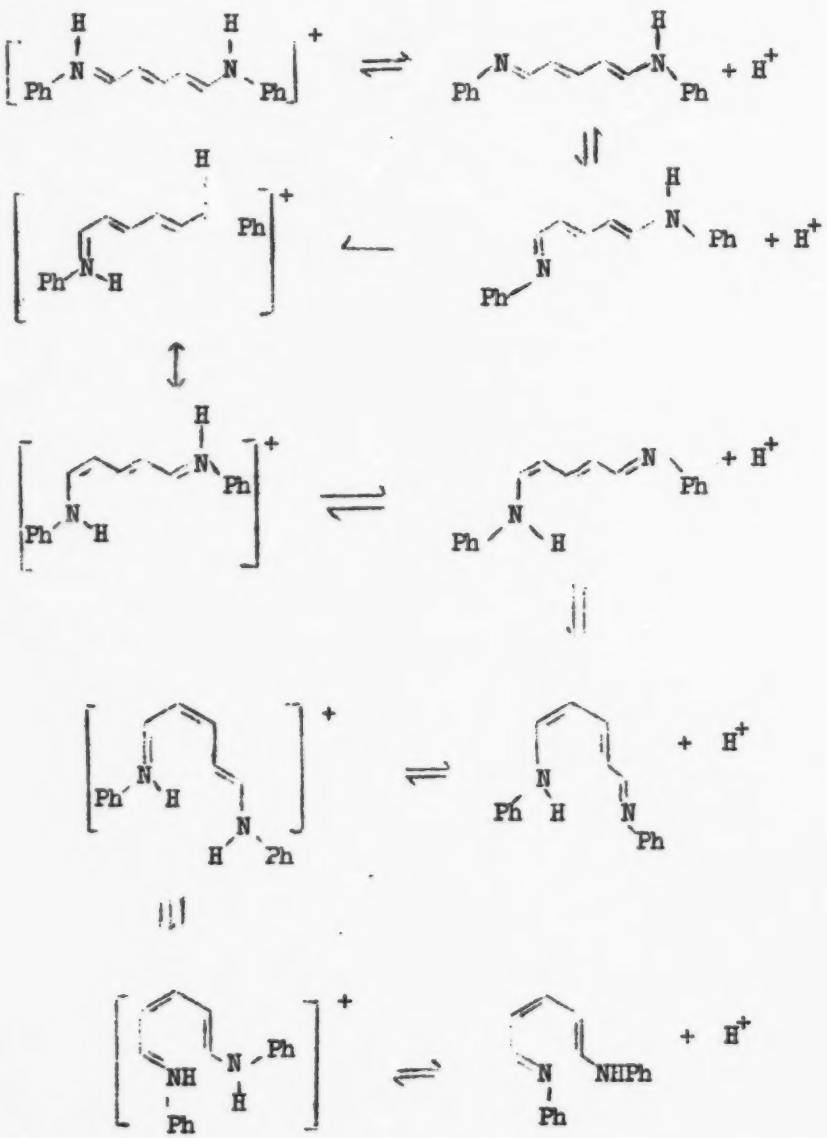
to be formed directly from V. Yet this unsymmetrical imino compound should be ideal as a substrate for the A mechanism.

These arguments do not constitute compelling evidence against mechanism A, but there does exist one experimental test which could perhaps distinguish between the two mechanisms, A and B. Reaction of II via A with step 2 rate determining (as is necessary if the rate is to be independent of base concentration) must involve a transition state with a large measure of charge separation. Generally valence isomerization reactions are not very sensitive in rate to solvent polarity.[9] The reaction was therefore carried out in a series of solvent mixtures varying from pure methanol to 80% dioxane-20% methanol. The rates are given in Table 3. One run carried out by adding a concentrated solution of I in methanol to a solution of excess triethylamine in dioxane gave a rate of 15.9×10^{-4} sec.$^{-1}$. A similar reaction run in dry acetone gave a rate of 5.81×10^{-4} sec.$^{-1}$. Isolation of the products of a macroscopic run in 80% dioxane-20% methanol showed that the reaction was unchanged by this solvent alteration.

Clearly the trend is established that the reaction proceeds more rapidly in less polar aprotic solvents than it does in a typical polar protic solvent like methanol. This provides further evidence against mechanism A and in favor of mechanism B. Further experiments are planned to provide further evidence vis-a-vis the differentiation between these two mechanisms.

Let us now turn to a discussion of the details of the present reaction process on the assumption that mechanism B is the most probable one. The most interesting question is--how does the linear chain attain the coiled conformation necessary for ring closure? The open-chain salt I is most

probably in the all-trans or stretched linear conformation, since x-ray studies have shown[10] that similar salts have this form. There are some published studies[11] which suggest these salts can undergo a facile change in conformation. However, it is not necessary to assume such a process in order to account for the required changes in conformation. A facile equilibrium between the salt I and free base II is sufficient alone to permit the conformational changes to take place with sufficient ease (see equations



above).

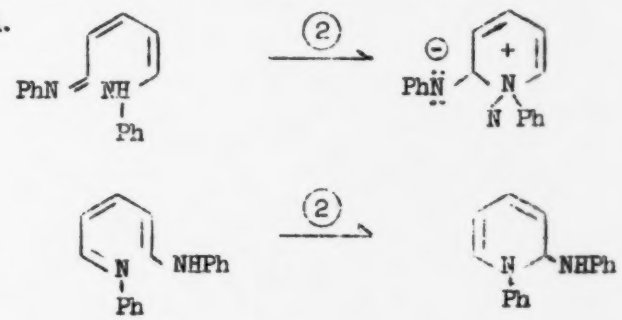
One consequence of either of these modes of accounting for the conformational interchange is that a pure base II, free of salt and kept in a nonprotic apolar solvent under strictly neutral conditions should be unable to undergo ring closure. Some experiments designed to test this assumption will be discussed in a later section of the report.

The question of the rate determining step is difficult to resolve cleanly. The kinetic data alone can be explained if step (2) is rate determining, or if step (5) is rate determining and the reaction is subject to general acid catalysis with solvent methanol playing the main role as the required acid. We have investigated the kinetics in buffer media of varying concentrations of benzoic acid while the benzoic acid/benzoate ion ratio was held constant. As Table 4 indicates the data are reasonably convincing of the lack of general acid catalysis. At present we feel the rate determining step is indeed the valence isomerization ring closure.

B. Influence of Substitution on the Rate of Ring Closure.

The evidence presented above showed that two possible mechanisms were acceptable. Of these mechanism B was preferred, but A could not be excluded. In each mechanism the evidence indicated that step (2) was the rate determining one in the process. The major difference between these two is that the

A.



transition state in A must involve a considerable degree of charge separation, while that in B does not. A symmetrically substituted derivative of I would be expected to show opposite effects at the two ends of the system in mechanism A. However since the rho value for the dissociation of anilinium ions in methanol is 3.02,[13] while that for the ionization of diphenylamines as acids is 4.07,[14] the effect of the group next to the negative nitrogen would be expected to dominate. The influence of substituents on the ring closure via route B has no published analog. However, all of the influence must be exerted by the group directly attached to the conjugated chain. Experiments are underway in our laboratories to establish the nature of this influence in an all carbon system.

A series of known symmetrically substituted salts[2,12] I a-d have been prepared by treating 2,4-dinitrophenylpyridinium chloride with the appropriate p-substituted aniline. These were all treated with an excess

I a Y = OMe
b Y = Me
c Y = Cl
d Y = F

of triethylamine in dry methanol and shown to undergo the ring closure reaction in high yield. In each case the substituted aniline was recovered and identified by spectral comparison with an authentic sample. The p-substituted phenylpyridinium salts were identified by melting point. Each of the salts Ia-d showed the expected visible spectra having two peaks in the region between 400 and 500 mμ. These were attributed to the salt and its free base, and the data shown in Table 5 were obtained by adding an excess of either anilinium chloride or triethylamine.

Ring closure rates for each of these salts were measured in dry methanol in the presence of an excess of triethylamine to assure that the rate plateau would be reached in all cases. Rates were obtained for four separate temperatures in each case and a sample of I itself was included to make certain that all were run under comparable conditions. The resultant data are shown in Table 6. From this information the activation parameters shown in Table 7 were calculated.

We can draw some conclusions from the data immediately. First and most important is the fact that substituents have only a small influence on the rate. Thus within the limits of the data all have $E_a = 23.1 \pm 1$ kcal./mole and $\Delta S^{\ddagger} = 0 \pm 1$ e.u. Interestingly the electron releasing substituents have almost no influence on the rate while electron attracting groups show a small rate enhancement. Studies of I y = NO_2 and I y = NMe_2 are underway. At present it is not possible to use this data to decide between the two candidate mechanisms.

C. Studies of the Base II in Aprotic Media.

The ability of the salt I to coil up into the proper conformation for ring closure must depend either on the symmetrical resonance hybrid nature of the salt I, or on the deprotonation-reprotonation scheme depicted earlier in this report. It is a consequence of either supposition that the free base II in pure form in an aprotic medium free from acidic or basic catalysts should be unable to isomerize to the appropriate cis isomer and thus should not undergo the ring closure. Zincke[2] has reported the isolation of the free base II as a light orange solid, m.p. 85-86°.

We have isolated the orange solid, m.p. 84-85°, but have found that it is not possible to remove all of the solvent under vacuum without decomposition

of the compound. When the purified solid is dissolved in carefully purified acetone under dried nitrogen the solution can contain only traces of water or methanol. Under these conditions II shows a sharp maximum at 388 mμ. A solution left in the ultraviolet spectrometer rapidly decolorizes; no band above 300 mμ is to be found at the conclusion of the run. The rate of disappearance of the 388 band is 3×10^{-4} sec.$^{-1}$ at 30°, compared with 5.4×10^{-4} sec.$^{-1}$ for a sample made by suspending I in dry acetone and adding excess triethylamine. However, the solution which results when II in acetone reacts in the spectrometer shows a very interesting behavior when removed from the spectrometer. After a few hours it turns yellow again and shows a visible spectrum having a band at 410 mμ.!

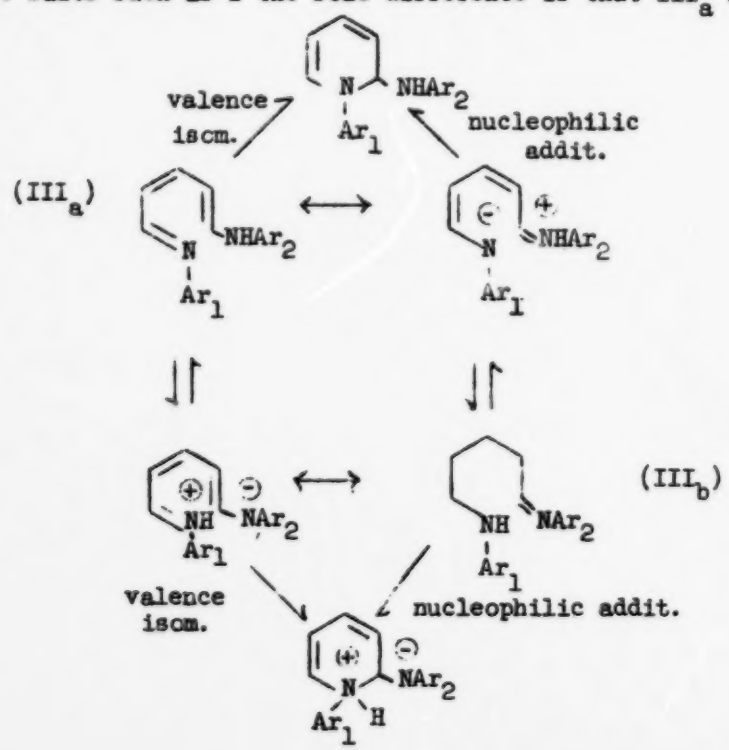
When a similar solution of II in acetone is allowed to stand in the laboratory at room temperature no color change is observed. However after several days the spectrum of the solutions shows no further absorption at 388 but only a sharp band at 410 mμ. Addition of anilinium chloride decreased to intensity of this band slightly, but when a few drops of hydrochloric acid were added the solution rapidly lost its color.

Finally two samples taken from the same solution were treated as follows. One sample was irradiated with tungsten light (150 watt bulb) while the other was stored in the dark. The sample stored in the dark was monitored by spectrophotometry and found to become colorless (no band above 330 mμ) initially, and after a longer time interval turned yellow with the 410 mμ band being responsible for the color. The irradiated sample rapidly became colorless, and after having been subjected to the same irradiation for three days, the solution remained colorless even after several days of storage in the laboratory.

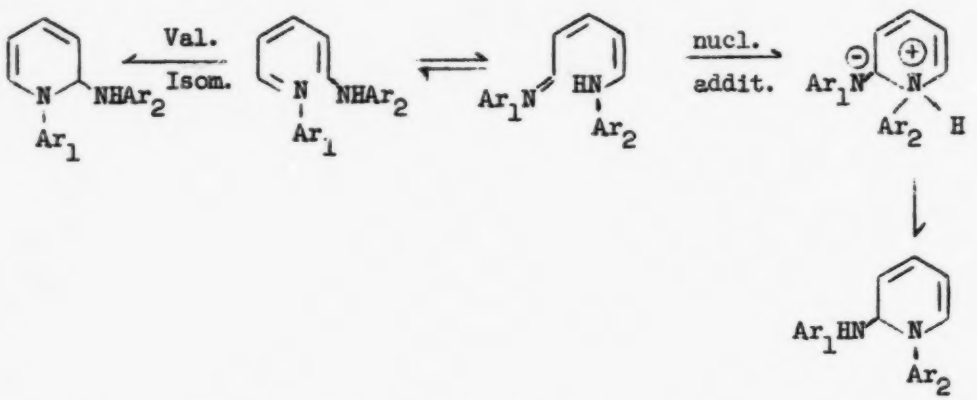
The data suggest that II undergoes a photochemical reaction which is reversed thermally. Also II undergoes a thermal process to give the substance with a 410 mμ peak. This latter reacts with acid to give a colorless substance. Investigation on layer samples is planned so that isolation and identification of these compounds can be accomplished.

D. Unsymmetrical Salts.

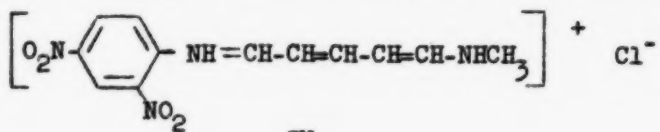
Perhaps the clearest distinction between the two mechanisms, A and B, can be made in terms of unsymmetrical salts. The scheme below shows that the question of whether to call the ring closure or ring opening process a valence isomerization or a nucleophilic addition is arbitrary and depends merely on the intuitive use of a term which relates to the major contributor to the resonance hybrid. The real question at issue is whether the protonated form III_a is the reactive species, or whether III_b is the reactive form. For symmetric salts such as I the sole difference is that III_a leads to an



uncharged dihydropyridine while III_b must give a product with charge separation. With an unsymmetrical molecule such as III it would be possible to design a molecule whose preferred protonation point could be predicted. Then the two processes would lead to different products as is illustrated below.



These unsymmetrical compounds are not readily accessible. In fact very few examples of the unsymmetrical salts have been reported. However, Zincke[1,2] did report that he was able to isolate the salt IV when



IV

2,4-dinitrophenylpyridinium chloride was treated with methylamine. We have repeated this and have been able to isolate this salt by working rapidly. However, it is very difficult to purify and to handle. It does undergo ring closure as described by Zincke and the products are methylpyridinium chloride and dinitroaniline. We are now studying the kinetics of this process.

Experimental

Spectra. - All ultraviolet spectra were determined in carefully purified or spectral grade solvents using a Cary Model 15 recording ultraviolet spectrometer equipped with a thermostatted cell compartment.

Solvents. - Methanol was dried by the method of Iund and Bjerrum, distilled and stored out of contact with moisture under nitrogen. Tetrahydrofuran was dried over calcium hydride, distilled from lithium aluminum hydride and stored under nitrogen. Dioxane was purified as described by Fieser and stored in the same manner as THF. Acetone was treated with potassium permanganate, distilled, passed through a column of neutral alumina, redistilled and stored under dry nitrogen.

König's Salts. - All salts were prepared by the method of Zincke[1] from 2,4-dinitrophenylpyridinium chloride. The salts are all known and their physical constants agree with literature values. They were recrystallized from methanol, dried in vacuo and used as described.

Kinetics. - For all kinetic runs with solutions of the salt containing less than enough added base to convert all the salt to its corresponding free base, an ampoule technique was employed. At various time intervals an ampoule was removed from the thermostatted bath, opened, a measured amount of a solution of anilinium chloride in methanol sufficient to convert all remaining substrate to the salt form was added and a properly diluted solution was analyzed by ultraviolet spectral measurements at 485 mμ.

For all kinetic runs with sufficient added base to ensure that all the substrate was present in the free base form, the reaction was carried out in a standard closed cell directly in the thermostatted cell compartment of the ultraviolet spectrometer. Analysis was made at 405 mμ.

Table I. Rates of Reaction of I in Methanol

Run No.	[M] I	[M] Base	Acid or Base	Temp.	Rate(sec.$^{-1}$)	Remarks
1	.000216	---	---	42.6	8.99×10^{-6}	
2	.000410	---	---	42.6	8.95×10^{-6}	
3	.000540	---	---	42.6	8.87×10^{-6}	
4	.000020	.000024	MeO^-	39.2	2.35×10^{-4}	
5	.000020	.000048	MeO^-	39.2	2.97×10^{-4}	
6	.000020	.000120	MeO^-	39.2	3.04×10^{-4}	
7	.000020	.000240	MeO^-	39.2	3.04×10^{-4}	
8	.000020	.00240	MeO^-	39.2	3.06×10^{-4}	
9	.0000204	.0000102	Et_3N	39.2	2.06×10^{-4}	
10	.0000204	.0000142	Et_3N	39.2	2.47×10^{-4}	
11	.0000204	.0000183	Et_3N	39.2	2.74×10^{-4}	
12	.0000202	.0000590	Et_3N	39.2	2.96×10^{-4}	
13	.0000202	.000117	Et_3N	39.2	3.08×10^{-4}	
14	.0000204	.000109	$(n\text{-}Bu)_3N$	39.2	3.05×10^{-4}	
15	.0000204	.000218	$(n\text{-}Bu)_3N$	39.2	3.18×10^{-4}	
16	.00053	.000154	$PhNH_3^+$	42.6	6.17×10^{-6}	curved plot
17	.000365	.00254	$PhNH_3^+$	42.6	6.13×10^{-6}	curved plot

Table 2. Rates of decomposition of I in methanol at 40.0° in the presence of various added bases. I is 0.000020 M.

Base	[M]	rate(sec.$^{-1}$)
MeO^-	.000020	3.24×10^{-4}
Et_3N	.000020	2.68×10^{-4}
Bu_3N	.000020	2.58×10^{-4}
MeO^-	.000010	2.30×10^{-4}
Et_3N	.000010	1.81×10^{-4}
Bu_3N	.000010	1.51×10^{-4}

Table 3. Rates of decomposition of I in mixed solvents at 30° in the presence of excess triethylamine.

Vol. % Dioxane	0	0	20	40	60	80
$k_1 \times 10^4$ sec.$^{-1}$	0.96	1.08	1.26	1.72	2.56	4.60

Table 4. Rates of decomposition of I in buffered solutions. [I] = 2.13×10^{-5} M [Et_3N] = 2.21×10^{-4} M. Temp. = 39.2°. Solvent 1% H_2O in methanol.

Run No.	Benzoic Acid [M] x 10^5	Sodium Benzoate [M] x 10^4	$LiClO_4$ [M] x 10^4	k x 10^4
1	2.13	2.03		2.77
2	1.60	1.52		2.71
3	1.06	1.01		2.84
4	----	----		2.75
5	1.60	1.52	.51	2.81
6	1.06	1.01	1.01	2.83
7	.231	.203	1.83	2.76
8	.106	.101	1.93	2.77
9	----	----	2.03	2.79

Table 5. Ultraviolet spectral properties of salts I a-d and their conjugate bases.

p-Subst.	Salt		Base	
	λ_{max}	E	λ_{max}	E
Me				
OMe	497	94,000	414	63,000
Cl	492	112,000	410	70,000
F	478	100,000	403	60,000

Table 6. Rates of ring closure of I a-d in dry methanol in the presence of excess triethylamine.

Compound	Rate $sec.^{-1} \times 10^5$			
	15°	20°	30°	40°
I b	1.22	2.30	8.65	31.0
I	1.31	2.65	9.91	35.3
I a	1.43	2.80	10.5	36.1
I c		4.78	17.6	61.6
I d		4.30	15.6	52.4

Table 7. Activation parameters for ring closure of salts I a-d.

Compound	E_a	$\Delta S^{\ddagger}$
I	23.3	0.0
I a	22.9	-1.3
I b	23.3	+0.2
I c	23.3	+0.9
I d	22.9	-0.3

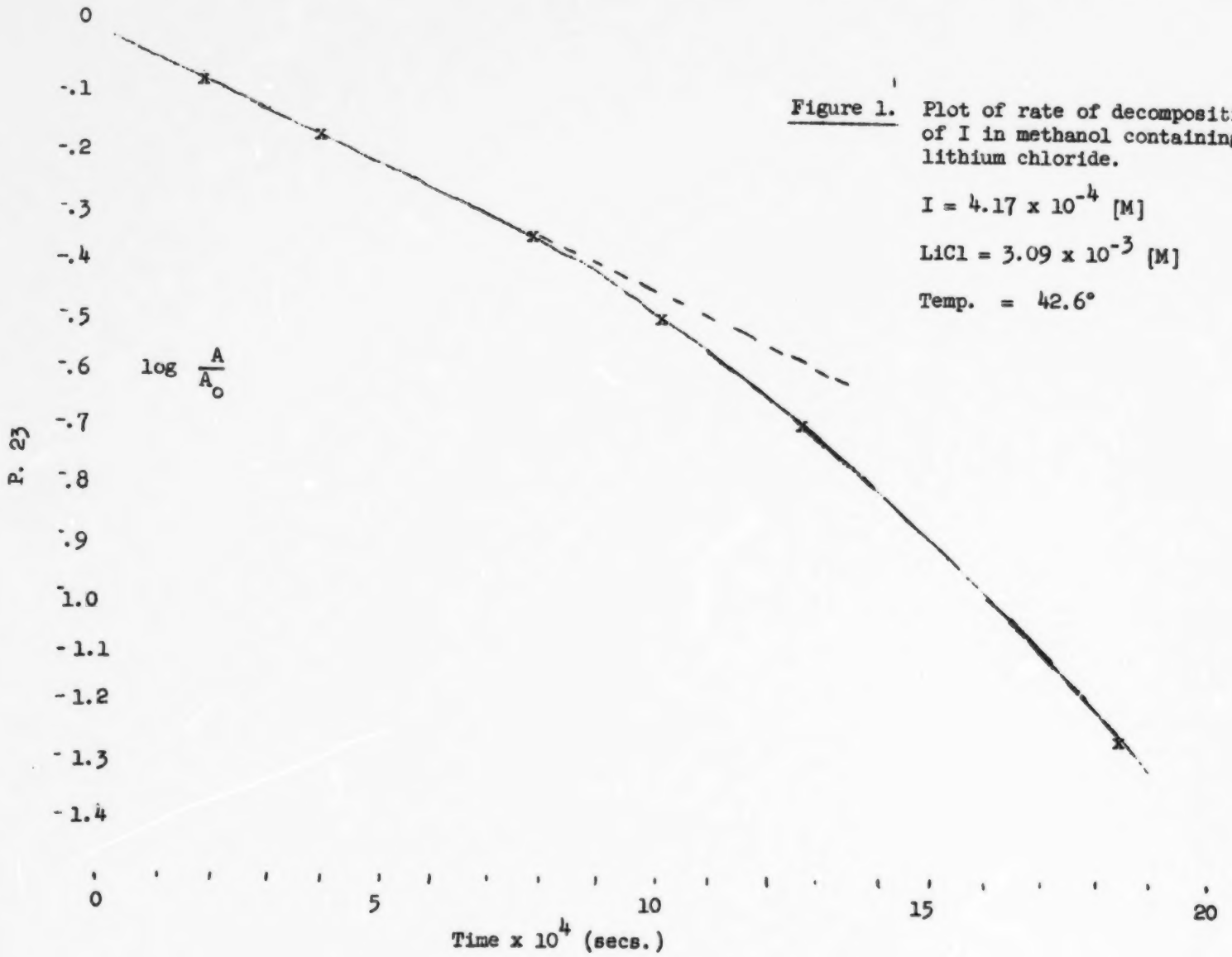


Figure 1. Plot of rate of decomposition of I in methanol containing lithium chloride.

$I = 4.17 \times 10^{-4}$ [M]

$LiCl = 3.09 \times 10^{-3}$ [M]

Temp. = 42.6°

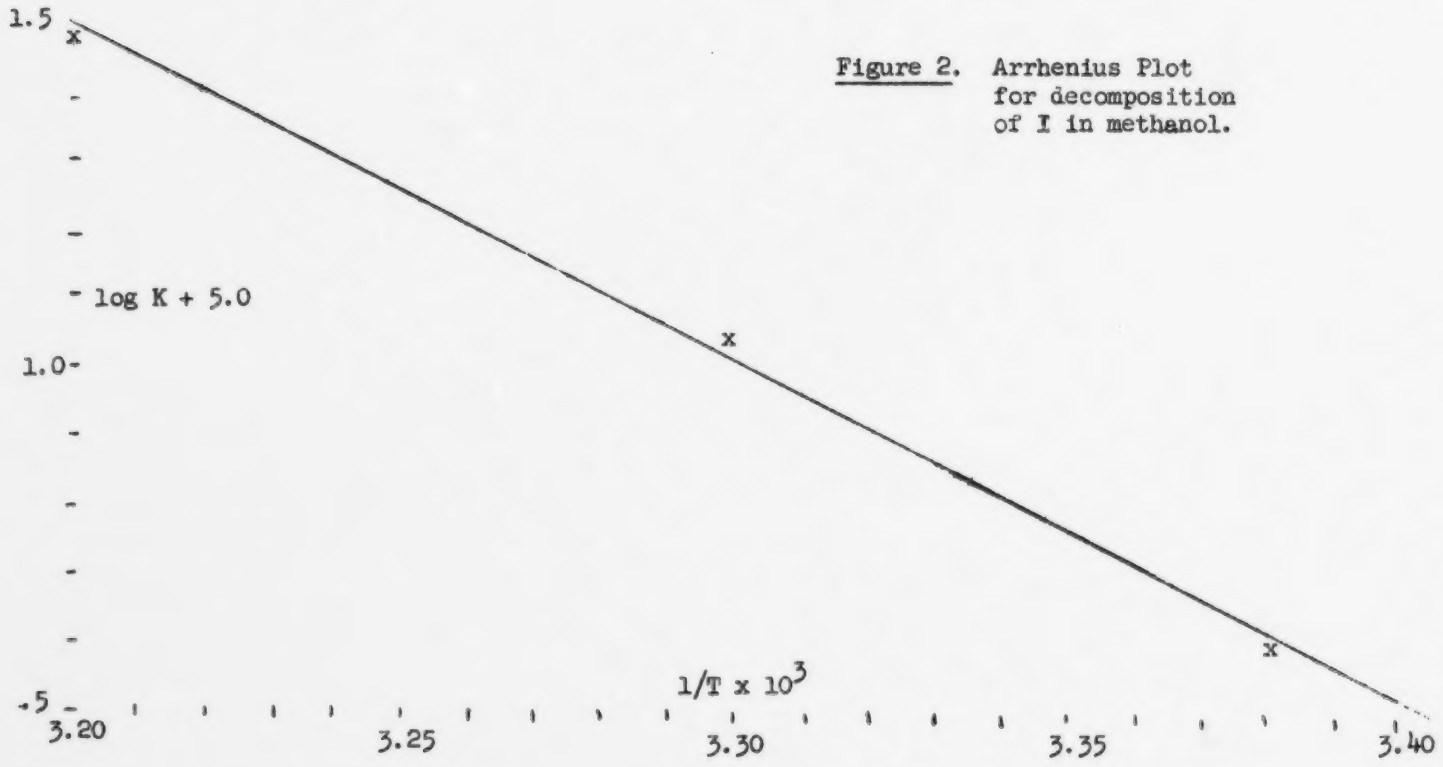


Figure 2. Arrhenius Plot for decomposition of I in methanol.

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Publication Plans

One preliminary communication on the mechanism of the ring closure of I in dry methanol has been published. A full

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account of this study will be submitted to either the Journal of the Americal Chemical Society or the Journal of Organic Chemistry in the immediate future. When one further example of the symmetrically substituted salts has been examined (Y = NO_2) a paper on the rate of reaction of substituted salts will be submitted to one of these two journals.